

## **REMARKS/ARGUMENTS**

Claims 28-58 and 82-88 are pending in this application, and presented for examination. Claims 56-58 and 85-87 have been amended. Claims 56-58 have been amended to depend from claim 28, the independent composition claim. Claims 85-87 have been amended to update their dependencies. No new matter has been entered and therefore, Applicants respectfully request entry of the foregoing amendments. Reconsideration is respectfully requested.

### **I. OBVIOUSNESS-TYPE DOUBLE PATENTING**

Claims 42-58 were rejected under the judicially created doctrine of obviousness-type double patenting for allegedly being obvious over claims 41 and 54-56 of U.S. Patent Application No. 08/889,355. Applicants respectfully request that the Examiner hold this rejection in abeyance until allowable subject matter is established. At that time, Applicants will take the necessary steps such as filing a terminal disclaimer to obviate the double patenting rejection.

### **II. REJECTION UNDER 35 U.S.C. §101**

The Examiner has rejected claims 56-58 under 35 U.S.C. § 101 as allegedly being the same subject matter as claims 1-3 of U.S. Patent No. 6,392,069 ("the '069 patent"). To the extent the rejection is applicable to the amended set of claims, Applicants respectfully traverse the rejection.

Claims 56-58 have been amended to be dependent on claim 28. Claim 28 is drawn to a composition for delivering an agent to a cell, which composition comprises an agent and a compound. As the '069 patent is drawn to compounds per se, the subject matter of claims 56-58, which is now drawn to compositions, is not identical. Therefore, the Examiner is respectfully requested to withdraw the rejection.

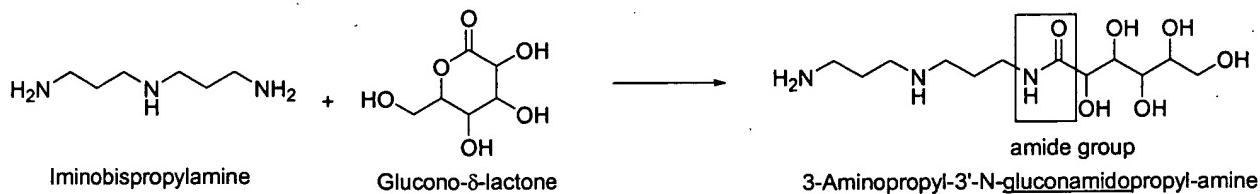
### III. REJECTION UNDER 35 U.S.C. §132

The Examiner has objected to the amendment filed March 29, 2002 as allegedly introducing new matter. More specifically, the Examiner states that as originally filed, X1, X2 and X3 are described as representing cholic acid and deoxycholic acid, but the structural formulae do not contain an acid group. In response, Applicants respectfully traverse the rejection.

Applicants respectfully assert that the structure of "a cholic acid group" is clear from the specification. For instance, Example 12 describes the synthesis of 3'-N-gluconamidopropyl-3"-N-cholamidopropyl-N-cholamide. Applicants submit that the chemical structure of the final product, Impurity II, and the intermediates leading to the final product would be readily apparent to one skilled in the art and unequivocally establishes the structure of a "cholic acid group."

For example, in Step 1 of Example 12, the specification teaches that one equivalent of glucono- $\delta$ -lactone is reacted with one equivalent of iminobispropylamine to form the amide product, 3-aminopropyl-3'-N-glucoamidopropyl-amine. The reagents specified in Step 1 are commercially available and would be known to a skilled artisan. As such, Applicants respectfully submit that one skilled in the art would immediately recognize that the reaction of the glucono- $\delta$ -lactone with iminobispropylamine will form the *amide* product, 3-aminopropyl-3'-N-glucoamidopropyl-amine as shown in Scheme 1.

Scheme 1:

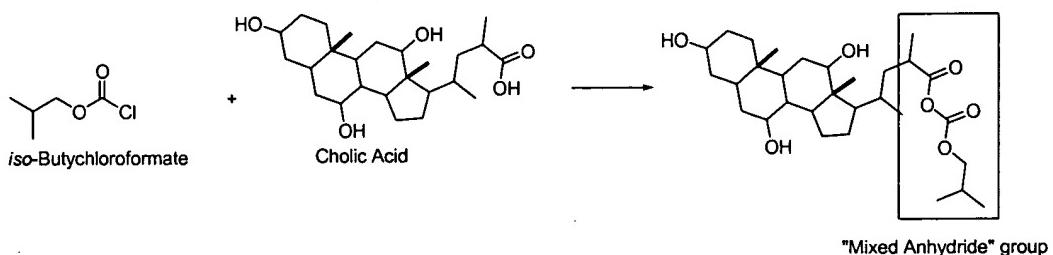


Furthermore, referring to Step 2 of Example 12, Applicants assert that one skilled in the art would immediately recognize that the reaction of the cholic acid (a carboxylic acid) starting material with isobutylchloroformate (an acid chloride derivative) will form a mixed anhydride intermediate (see, Scheme 2 below). Applicants note that *iso*-butylchloroformate and

cholic acid are both commercial reagents, the structures of which would be readily apparent to a skilled artisan. Subsequent reaction of the mixed anhydride intermediate with 3-aminopropyl-3'-N-glucoamidopropyl-amine (an amine), will result in the formation of the amide bonds of Impurity II in which the carbonyl group of the amide group will have originated from the cholic acid starting material as depicted below in Scheme 3.

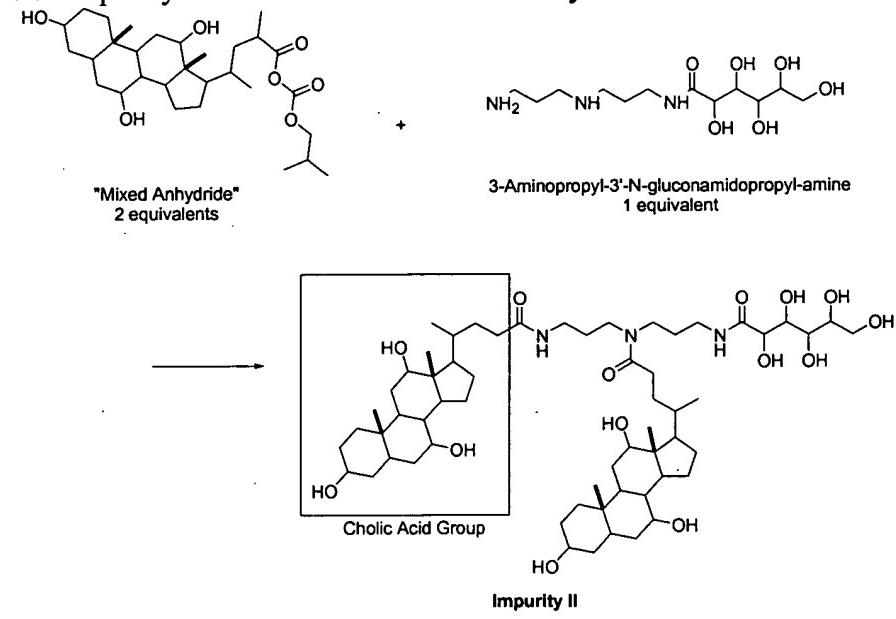
Scheme 2:

Synthesis of the "Mixed Anhydride"



Scheme 3:

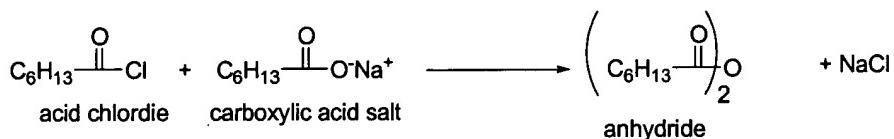
Synthesis of Impurity II: Reaction of the mixed anhydride with the amine from Step 1.



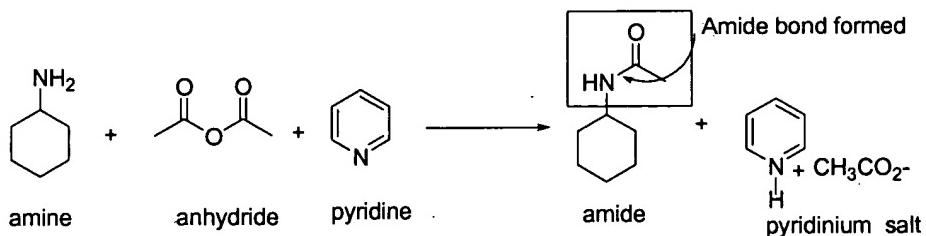
In this instance, Applicants submit that the chemical reactions used in Example 12 are common synthetic transformations well known to one skilled in the art as shown by the fact that an analogous set of transformations is described in introductory organic textbooks titled

"Introduction to Organic Chemistry".<sup>1</sup> The following reactions are described therein: 1) the reaction of an acid chloride derivative and a carboxylic acid to form an anhydride; and 2) the reaction of an anhydride with an amine. Relevant sections from the textbook are reproduced in Schemes 4 and 5 (below) for the Examiner's convenience.

Scheme 4: Reaction of an acid chloride with a carboxylic acid.



Scheme 5: Reaction of an anhydride with an amine.



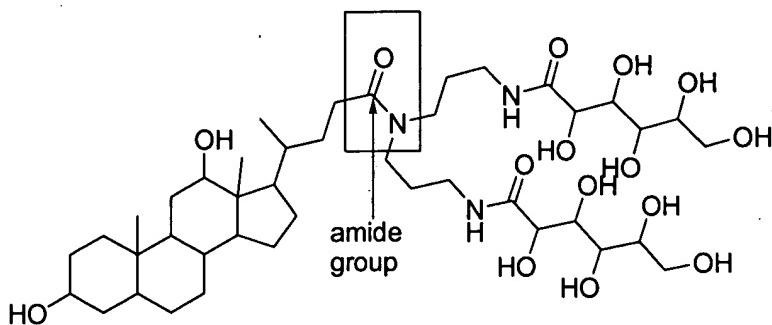
As such, based on the experimental procedure (*i.e.*, reagents used and the description of the resultant intermediates) provided in Example 12, Applicants assert that a skilled artisan attempting to practice the present invention would readily recognize the chemical structures of the intermediates and more importantly, the attachment of the "cholic acid group" to impurity II. In view of the above, Applicants submit that the original specification teaches the structure of a "cholic acid group" and its attachment to a compound of Formula I.

Further, Applicants respectfully assert that a skilled artisan would recognize that "cholic acid" is attached to Formula I to form an amide group. Additional evidence supporting Applicants' assertion of the manner in which the cholic acid group is attached to Formula I can be found in the chemical name of Impurity II. Example 12 teaches that the name of Impurity II is 3'-N-gluconamidopropyl-3"-N-**cholamidopropyl**-N-**cholamide**. A skilled artisan would recognize from the name of Impurity II that the cholic acid group is attached via an **amide** group. As support, Applicants respectfully point out Big Chap is sold commercially under the name,

<sup>1</sup> See Exhibit: Introduction to Organic Chemistry, 4th Ed.; 1992; Prentice-Hall, Inc., pgs. 530-531.

**N,N-bis-(3-D-Gluconoamidopropyl)deoxycholamide.** In the name of Big Chap, the "cholamide" group refers to a cholic acid group in Big Chap wherein the carboxylic acid group of cholic acid is replaced with an amide group. The structure of Big Chap is shown below (see, Scheme 6).

Scheme 6



**N,N-bis-(3-D-Gluconoamidopropyl)deoxycholamide**

**"Big CHAP"**

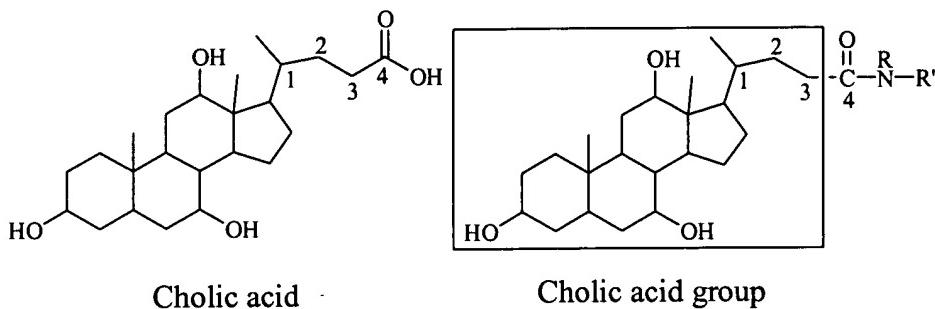
In view of the above, Applicants submit that the specification provides a significant amount of support for the amendment and the structure of a "cholic acid group." As such, Applicant respectfully requests that the Examiner withdraw the new matter rejection.

#### **IV. REJECTION UNDER 35 U.S.C. §112, FIRST PARAGRAPH**

The Examiner has rejected claims 28-55 and 82-88 for allegedly failing to comply with the written description requirement. More specifically, the Examiner states that the structural formula representing the variables X1, X2 and X3 are described as representing cholic acid and deoxycholic acid, but the structural formulae do not contain an acid group. In response, Applicants respectfully traverse the rejection.

To a person skilled in the art, it is abundantly clear that the phrase a "cholic acid group" means that it is not a cholic acid any longer, but rather a derivative of cholic acid. Applicants respectfully point out that a "cholic acid group" has had the terminal CO<sub>2</sub>H substituted. Following the synthetic procedures in schemes 1-3 on pages 12 and 13 above, it is abundantly clear that the cholic acid group has the structure set forth in scheme 3. In fact,

comparing the two structures below of “cholic acid” and “a cholic acid group”, the Examiner can plainly see that the only difference is the atoms used in the connectivity of the cholic acid group to Formula I.



As set forth in MPEP § 2111.02:

Applicant may be his or her own lexicographer as long as the meaning assigned to the term is not repugnant to the term's well known usage. *In re Hill*, 161 F.2d 367, 73 USPQ 482 (CCPA 1947). Any special meaning assigned to a term "must be sufficiently clear in the specification that any departure from common usage would be so understood by a person of experience in the field of the invention." *Multiform Desiccants Inc. v. Medzam Ltd.*, 133 F.3d 1473, 1477, 45 USPQ2d 1429, 1432 (Fed. Cir. 1998).

Applicants are allowed to be their own lexicographer and define a term in a manner that would be sufficiently clear in the specification and understood by a person of experience in the field. In the instant case, Applicants have chosen to define the term “cholic acid group” as cholic acid without the terminal CO<sub>2</sub>H. This is clearly well within Applicants’ rights, and would be understood by a person skilled in the art. For example, when Applicants set forth “cholic acid group” in the specification on page 9, line 8, this would be read in conjunction with Example 12. Example 12 clearly states that cholic acid is reacted with isobutylchloroformate in the presence of triethylamine, followed by reaction with 3-aminopropyl-3’-N-gluconamidopropyl-amine to afford Impurity II. Clearly, this would be understood by a person skilled in the art.

Moreover, after reviewing several patent documents (such as U.S. Patent Nos. 5,856,202; 4,892,816; 4,458,015) wherein “cholic acid group” is used, in no instance does it state that “cholic acid” is the same as “a cholic acid group”. Thus, the Examiner’s insistence that “cholic acid group” means “that the moiety contains an acid functionality” is contrary to the

Appl. No. 10/055,863  
Amdt. dated May 5, 2005  
Office Action dated December 13, 2004

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clear meaning of cholic acid group in this application and the patent literature. As such, Applicants respectfully request that the Examiner withdraw the rejection.

**V. REJECTION UNDER 35 U.S.C. §112, SECOND PARAGRAPH**

The Examiner rejected claims 85-88 under 35 U.S.C. § 112, second paragraph as allegedly being indefinite. Claims 85-87 have been amended to update their dependency. In view of the amendments to the claims, Applicants respectfully request that the Examiner to withdraw the rejection.

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5000.

Respectfully submitted,



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